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EXAMINER

NOGUEROLA, ALEXANDER STEPHAN

ART UNIT	PAPER NUMBER
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1753

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/874,331	Applicant(s) LIU ET AL. S.C.	
	Examiner ALEX NOGUEROLA	Art Unit 1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 6/01/2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4,6-9,11-24 and 26-37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-4,6-9,11,18-20 and 34-37 is/are allowed.
- 6) ☒ Claim(s) 12-17,21-24 and 26-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>06012004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Objections

1. Claim 18 is objected to because of the following informality: in line 9 "a" should be deleted.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 12-17, 21-24, and 26-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention:

a) Claim 12, lines 11-12: how can the *substantially isolated* separation channels be of the *same* separation channel?

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b) Claim 12: the antecedent bases for the first sample component and the plurality of second sample components are not clear. Applicants' should clarify that the first sample component and the plurality of second sample components are the result of "obtaining a first separation of the sample components" from the sample. Perhaps -- into a first sample component and a plurality of second sample -- can be inserted between "sample" and "components" in line 3;

c) Claim 12: how can there be more than one "second" sample component?

d) Claim 21: it is not clear that the plurality of second, substantially isolated volumes is a subset of the plurality of substantially isolated volumes resulting from the electrophoresis separation. Applicants' should clarify the relationship between the plurality of second, substantially isolated volumes and the plurality of substantially isolated volumes resulting from the electrophoresis separation;

e) Claim 21: does "the isolated volumes" in the last line of the claim refer to both the "at least one of the substantially isolated volumes" and the "plurality of second, isolated volumes"?

f) Claim 22 recites the limitation "the other sample components" in line 3. There is insufficient antecedent basis for this limitation in the claim;

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g) Claim 24 recites the limitation "the peak" in line 3. There is insufficient antecedent basis for this limitation in the claim;

h) Claim 26 recites the limitation "the first substantially isolated volume" in line 2. There is insufficient antecedent basis for this limitation in the claim;

i) Claim 26 recites the limitation "each fraction" in line 2. There is insufficient antecedent basis for this limitation in the claim;

j) Claim 27: how can there be more than one "second," substantially isolated volume?

k) Claim 27: how are the "plurality of second, substantially isolated volumes" related to the "at least one of the substantially isolated volumes"?

l) Claim 28: the relationship between the fractions collected by the autosampler and the first sample component and second sample component are not clear. Are the first sample component and the second sample component fractions collected by the autosampler?

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m) Claim 29: it is not clear whether there is a relationship between the fractions resulting from the separation by the first separation component and the sample component. Is the first sample component a component of a sample fraction?

4. Note that dependent claims will have the deficiencies of base and intervening claims.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 29-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Isaaq et al. (*Electrophoresis* 199, 20, 1533-1537), hereafter "Isaaq et al.," in view of Kane et al. (US 5,916,428), hereafter "Kane," and the JPO abstract of Sonoda et al. (JP 64-80852 A), hereafter "Sonoda."

Addressing claim 29, Isaaq et al. discloses a separation system, comprising

a first separation component for separating a sample into a plurality of fractions, wherein the first separation can be performed in the absence of an applied electro field (abstract; 2.2 Instrumentation on page 1534);

an isolated separation lane, the system configured to electrophoretically separate each fraction along the isolated separation lane (abstract and 2.3.4 Method on page 1535);

a detector to detect the presence of (a) a sample component and (b) a reference standard migrating along the isolated separation lane (2.3.3 CZE conditions on page 1534 and 3. Results and discussion on page 1535); and

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a processor configured to correct a migration time of the sample component from the separation lane for migration time variations between runs based upon a migration time of the reference standard (2.3.3 CZE conditions on page 1534).

Isaaq et al. does not *describe in detail* an embodiment of the separation system having a plurality of isolated separation lanes. Kane et al. disclose a separation system comprising a plurality of isolated separation lanes, the system configured to electrophoretically separate each of numerous sample fractions along each of the isolated separation lanes (abstract and Figures 1 and 2A). It would have been obvious to one with ordinary skill in the art at the time the invention was made to use a plurality of isolated separation lanes as taught by Kane et al. in the invention of Isaaq et al., instead of just one isolated separation lane, because then, as taught by Isaaq et al., multiple sample fractions can be analyzed simultaneously and without supervision (second paragraph of 3.1 On-line vs. off-line: advantages and limitations, which begins on page 1536).

Isaaq et al. as modified by Kane et al. does not *mention* a processor configured to correct a migration time of the sample component from at least a first one of the isolated separation lanes for migration time variations between the isolated separation lanes based upon a migration time of the reference standard from at least one other isolated separation lanes. It would have been obvious to one with ordinary skill in the art at the time the invention was made to so configure the processor because, as stated above, Isaaq et al. discloses a processor configured to correct a migration time of the sample component from the separation lane for migration time variations between runs based upon a migration time of the reference standard (2.3.3 CZE conditions on page

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1534). One with ordinary skill in the art would have recognized that comparing the migration times of reference markers in several runs occurring simultaneously in several isolated separation lanes is effectively the same as comparing the migration times of a reference marker in two or more sequential separations in the same separation lane.

In the alternative, Sonoda et al. discloses a processor configured to correct a migration time of a sample component in at least a first one of several isolated separation lanes for migration time variations between the isolated separation lanes based upon a migration time of a reference standard from at least one other isolated separation lanes (abstract). It would have been obvious to one with ordinary skill in the art at the time the invention was made to configure the processor as taught by Sonoda et al. in the invention of Isaaq et al. as modified by Kane et al. because this will improve the accuracy of the analysis of the resulting separation data (such as peak interpretations of electropherograms)

Addressing claim 30, Isaaq et al. discloses an autosampler (second paragraph of 3.1 On-line vs. off-line: advantages and limitations, which begins on page 1536).

Addressing claim 31, Isaaq et al. discloses normalizing (correctly with a calculated delay coefficient) the migration time of a sample component in one of the isolated separation lane based on a reference standard in another separation lane.

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Addressing claim 32, that peak indicative of the reference standard is identified is implied since its migration time is recorded (see the Sondo abstract and also consider 3. Results and discussion in Isaaq, which discusses an electropherogram having a reference marker peak).

Addressing claim 33, Isaaq et al. as modified by Kane et al. discloses a plurality of isolated capillaries.

Allowable Subject Matter

9. Claims 1-4, 6-9, 11, 18-20, and 34-37 are allowed.
10. Claims 12, 21, 27, and 28 would be allowable if rewritten or amended to overcome the rejections under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action.
11. Claims 13-17, 22-24, and 26 would be allowable if rewritten to overcome the rejections under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

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12. The following is a statement of reasons for the indication of allowable subject matter:

a) Claims 1, 18-20, and 34: the nonobvious limitation in the combination of limitations in each of claims 1, 18-20, and 34 is the requirement that the second peak (or reference standard peak, for claim 34) for each isolated channel (or capillary, for claim 34) be in the same intensity-time record as the first peak. One with ordinary skill in the art would understand an "intensity-time record" to be an electropherogram or similar type record for a sample component (or fraction, for claim 34) after undergoing the second separation (see the last paragraph on page 2 of Applicants' specification). That is, that the first peak and the second peak (or reference standard peak) arise from co-migrating constituents of the same sample component (or fraction) undergoing the second separation.

Isaaq et al. (*Electrophoresis* 1999, 20, 1533-1537) as modified by Kane et al. (US 5,916,428) and the JPO abstract of Sonoda et al. (JP 64-80852 A) discloses a first separation (or first separation component, for claim 18, or chromatographic separation, for claim 34) and a second separation (or an electrophoresis component, for claim 18, or electrophoretic separation for claims 20 and 34) as claimed; however, a migration time of at least one of the first peaks is normalized with respect to a delay coefficient based on a plurality of second peaks obtained from intensity-time data records created *separately* from any intensity-time data record containing a first peak. In Sonoda et al. a reference marker is electrophoresed in each of several electrophoresis lanes and an intensity-time data record created for each reference marker run. Each of these intensity-time data records contains a "second peak," which corresponds to the reference marker. Next a

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delay coefficient is calculated based on all of the second peaks. Then a sample is electrophoresed in each lane for each of which an intensity-time record is created, which each have a "first peak" corresponds to an analyte of interest. Thus, in Isaaq et al. as modified by Kane et al., and Sonoda et al. the "second peaks" ("reference standard peaks") are from intensity-time data records created before and separately from any intensity-time data record having a "first peak."

b) Claims 2-4 depend directly or indirectly from allowable claim 1.

c) Claim 6: the nonobvious limitation in the combination of limitations in is the requirement of "normalizing an intensity of at least one of the first peaks with respect to an average intensity of a plurality of the second peaks to correct for the intensity differences between the isolated channels."

Isaaq et al. (*Electrophoresis* 1999, 20, 1533-1537) as modified by Kane et al.

(US 5,916,428) and Liu et al. (US 5,228,960) normalize an intensity of at least one of the first peaks by either shifting the baseline of the intensity-time data records so that they all have a common horizontal baseline or by adjusting the intensity of the first peak relative to another peak from the same intensity-time data record (in Liu et al. see col. 8, ll. 28-51).

c) Claims 7-9 and 11 depend directly or indirectly from allowable claim 6.

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d) Claim 12: the nonobvious limitation in the combination of limitations in is the requirement of “a processor configured to normalize a migration time of a first sample component within at least one of the separation channels with respect to an average migration time of each of a plurality of respective second sample components, the respective sample components having been separated along different ones of the substantially isolated separation channels of the same separation channel to adjust for migration time differences between the isolated channels.”

Isaaq et al. (*Electrophoresis* 1999, 20, 1533-1537) as modified by Kane et al. (US 5,916,428) and the JPO abstract of Sonoda et al. (JP 64-80852 A) discloses a first separation component and a second separation component as claimed; however, a processor normalizes the migration time of a first sample component using a delay coefficient based on the migration times for another sample component that is from a different sample than from which the first sample component originates. In Sonoda et al. before a sample containing an analyte is electrophoresed a reference marker is electrophoresed in each of several electrophoresis lanes and an intensity-time data record created for each reference marker run. Thus, the reference marker and the sample containing analyte are not sample components from the same sample.

e) Claim 21: the nonobvious limitation in the combination of is the requirement of “normalizing a migration time of at least one of the substantially isolated volumes with respect to an average migration time of a plurality of second, substantially isolated volumes to correct for migration time difference between the isolated volumes.” The at

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least one of the substantially isolated volumes and the second, substantially isolated volumes originate from the same sample.

Isaaq et al. (*Electrophoresis* 1999, 20, 1533-1537) as modified by Kane et al. (US 5,916,428) and the JPO abstract of Sonoda et al. (JP 64-80852 A) discloses a first separation and a second separation as claimed; however, a migration time of at least one of the first peaks is normalized with respect to a delay coefficient based on a plurality of second peaks obtained from intensity-time data records created *separately* from any intensity-time data record containing a first peak. In Sonoda et al. a reference marker is electrophoresed in each of several electrophoresis lanes and an intensity-time data record created for each reference marker run. Each of these intensity-time data records contains a "second peak," which corresponds to the reference marker. Next a delay coefficient is calculated based on all of the second peaks. Then a sample is electrophoresed in each lane for each of which an intensity-time record is created, which each have a "first peak" corresponds to an analyte of interest. Thus, in Isaaq et al. as modified by Kane et al., and Sonoda et al. the "second peaks" are from intensity-time data records created before and separately from any intensity-time data record having a "first peak." In short, what corresponds to the at least one of the substantially isolated volumes in Isaaq et al. as modified by Kane et al. and Sonoda et al. would not originate from the same sample as that from which what correspond to the second, substantially isolated volumes originate.

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f) Claim 27: the nonobvious limitation in the combination of limitations in is the requirement of “normalizing an intensity of at least one of the substantially isolated volumes with respect to an average intensity of a plurality of second, substantially isolated volumes to correct for the intensity differences between the isolated volumes.”

Isaaq et al. (*Electrophoresis* 1999, 20, 1533-1537) as modified by Kane et al.

(US 5,916,428) and Liu et al. (US 5,228,960) normalize an intensity of at least one of the substantially isolated volumes by either shifting the baseline of the intensity-time data records for the first plurality of sample components so that they all have a common horizontal baseline or by adjusting the intensity of the peak corresponding to the at least one of the substantially isolated volume relative to a peak corresponding to another substantially isolated volume from the same intensity-time data record (in Liu et al. see col. 8, ll. 28-51).

g) Claim 28: the nonobvious limitation in the combination of limitations is the requirement of “a processor configured to normalize a migration time of a first sample component within at least one of the separation channels with respect to a migration time of at least a second sample component, to adjust for migration time difference between the isolated channels.” The first sample component and the second sample component originate from the same sample.

Isaaq et al. (*Electrophoresis* 1999, 20, 1533-1537) as modified by Kane et al.

(US 5,916,428) and the JPO abstract of Sonoda et al. (JP 64-80852 A) discloses a first separation and a second separation as claimed; however, a migration time of at least one

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of the first peaks is normalized with respect to a delay coefficient based on a plurality of second peaks obtained from intensity-time data records created *separately* from any intensity-time data record containing a first peak. In Sonoda et al. a reference marker is electrophoresed in each of several electrophoresis lanes and an intensity-time data record created for each reference marker run. Each of these intensity-time data records contains a "second peak," which corresponds to the reference marker. Next a delay coefficient is calculated based on all of the second peaks. Then a sample is electrophoresed in each lane for each of which an intensity-time record is created, which each have a "first peak" corresponds to an analyte of interest. Thus, in Isaaq et al. as modified by Kane et al., and Sonoda et al. the "second peaks" are from intensity-time data records created before and separately from any intensity-time data record having a "first peak." In short, what corresponds to the first sample component in Isaaq et al. as modified by Kane et al. and Sonoda et al. would not originate from the same sample as that from which the second sample component originates.

h) Claims 35-37 depend from allowable claim 34.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Alex Noguerola
Primary Examiner
AU 1753
August 8, 2004